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Subject: Environmental Defense comments on Sulfuric Acid, Diethyl Ester (CAS# 64-67-5)

(Submitted via Internet 6/25/04 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and Ehunt@adelphia.net)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for Sulfuric Acid, Diethyl Ester (CAS# 64-67-5).

The test plan and robust summaries for sulfuric acid, diethyl ester, also termed diethyl sulfate (DES), were submitted by Dow Chemical Company. DES is used in a wide variety of intermediates and products, including in surfactants, dyes, agricultural chemicals and pharmaceuticals. It is used in the manufacture of fabric softeners in detergents, hair care applications, disinfectants, drilling fluids, lubricants, oil-based paints, corrosion inhibitors and many other products. The workplace exposure guideline is 1 ppm as an 8-hr time-weighted average. Monitoring data indicate that short-term exposures of as high as 1.8 ppm have occurred.

The sponsor states that, based on its use as a chemical intermediate and the rapid hydrolysis of any residual DES from production, no significant exposures to consumers is anticipated to occur. While this may be true, are data available regarding the presence or absence of DES or its major degradation products in consumer or industrial products, waste streams or air emissions?

The test plan and robust summaries are complete and informative. The sponsor notes that additional studies are needed for stability in water. Although there are no existing repeat dose, reproductive or developmental toxicity studies, the sponsor argues that they are not needed because DES is a probable human carcinogen and the production, labeling and handling of DES are specifically designed to minimize exposure to carcinogenic agents. This argument is inconsistent with the HPV program, which requires data on all SIDS endpoints. Positive toxicity data for one endpoint does not negate the need to provide data for other endpoints. We also note that exposure limits for carcinogens are often set as annualized averages, whereas exposure limits for non-cancer endpoints may have much shorter averaging times, so non-cancer endpoints may drive risk assessments and risk management measures needed in some exposure circumstances. This is the case, for example, for formaldehyde among other chemicals. Therefore, we disagree with the sponsor and we recommend that a combined reproductive/developmental/repeat dose study be conducted on DES. If the existing animal cancer studies included interim sacrifices and appropriate histological analyses, then these data would be adequate to cover the repeat dose endpoint.

The three aquatic toxicology endpoints are proposed to be met by experimental data in fish and ECOSAR modeling for aquatic invertebrates and algae. The test plan includes an interesting discussion on a testing

strategy for these endpoints. The sponsor states that if the proposed water stability studies indicate that DES is rapidly converted to sulfuric acid and ethanol (as suspected) then the ECOSAR data should be adequate. However, if the conversion occurs more slowly than expected and significant amounts of ethyl sulfate are formed then new studies on aquatic invertebrates and algae will be performed, as the ECOSAR models would not be relevant to such a situation. We agree with this rationale and compliment the sponsor in presenting it in an understandable manner. However, we were puzzled that the sponsor presented the same strategy for fish toxicity data. Since the fish studies represent actual experimental data (a 96-hr study), which presumably already reflects either a rapid or slow conversion to sulfuric acid and ethanol, why would new studies be needed under either scenario? Are there other deficiencies in this study that would warrant repeating it?

Other comments are as follows:

1. The robust summaries include descriptions of the available cancer epidemiology data, which indicate that upper respiratory tract cancers may be increased by occupational exposures to DES. This information, although not explicitly required by the HPV program, is helpful.

2. DES is a potent genotoxin in both in vitro and in vivo studies. Is this a consequence of sulfuric acid actions?

3. Existing data indicate that DES is readily biodegradable and therefore it should not accumulate in the environment.

Thank you for this opportunity to comment.

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